

$^{68}\text{Ge}/^{68}\text{Ga}$ radioisotope generator as a source of radiotracers for water flow investigations

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Abstract. Radiotracer experiments on the model of rectangular settler with a volume of 3 m³, with a consecutive application as a tracer of the aqueous phase fluoresceine (representative tracer of water), eluate from a $^{68}\text{Ge}/^{68}\text{Ga}$ radioisotope generator (0.1 N HCl solution) and chelates after Ga ions complexation with 1,4,7-triazacyclononane-1,4,7-triacetic acid (NOTA) and 1,4,7,10-tetrazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) were carried out. The obtained residence time distribution (RTD) functions indicate that only the complex compounds of gallium are stable in the water phase and are not adsorb on the vessel walls, so they can be recommended as tracers of the water phase.

Key words: Ga-68 • generator • residence time distribution (RTD)

Introduction

Radioisotopes are widely used as tracers throughout industries to optimize processes, to solve problems concerning the flow structure inside the apparatus under investigation and to improve the quality and yield of final process products. However, the radiotracer routine services are in many cases limited by difficulties with the availability of radioisotopes. Many countries have no radioisotope production facilities like nuclear reactors or cyclotrons for target material irradiation.

A similar problem has occurred in nuclear medicine, therefore for medical purposes, alternative sources of radiotracers – medical radionuclide generators were elaborated. In principle, a radionuclide generator is a device that is based on the mother-daughter genetic relationship and allows for the separation and extraction (elution) of a short-lived daughter isotope from the long-lived stationary mother [2]. The mother radionuclide is firmly adsorbed in a support material (exchange resin, etc.) which is packed in a small column. The daughter radionuclide is eluted from the system by suitable solvents (elutants). Actually, more frequently are used such generators as $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ and $^{113}\text{Sn}/^{113\text{m}}\text{In}$, but these daughter radionuclides have limited applications in industrial and environmental studies because of their relatively low gamma energy and some other limitations connected with chemical properties of TcO_4^- and In^{+3} ions in water solutions (tendency to adsorption on the vessel walls and surface of particles presented in water).

Nevertheless, some applications of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators for environmental investigations were presented [1, 4]. The authors of these works have stated that the

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Table 1. The nuclear characteristics of $^{68}\text{Ge}/^{68}\text{Ga}$ generator

Generator	Production	Mother nuclide			Daughter nuclide		
		Half-life	Decay	γ (keV)	Half-life	Decay	γ (keV)
$^{68}\text{Ge}/^{68}\text{Ga}$	$^{69}\text{Ga}(p,2n)^{68}\text{Ge}$	270 d	EC	–	1.135 h	β^+	511, 1077

phenomena of tracer sorption on vessel walls are observed, if the eluate from generators is directly used as a tracer of water phase.

For a radionuclide generator to be suitable for industrial use, some criteria need to be satisfied:

- Half-life of the mother radionuclide must be appropriately long (more than several months).
- Half-life of the daughter radionuclide may vary from several minutes to several hours.
- Gamma-ray emitters are preferred because the ability of gamma radiation to penetrate the walls of a vessel under investigations.

Taking into account the above criteria, some new nuclear mother/daughter relationships have been found to be suitable for production of radiotracers for industrial use, i.e. $^{68}\text{Ge}/^{68}\text{Ga}$; $^{137}\text{Cs}/^{137}\text{Ba}$ and others [2]. Actually, both the $^{68}\text{Ge}/^{68}\text{Ga}$ and $^{137}\text{Cs}/^{137}\text{Ba}$ generators are commercially available. Taking into account the nuclear characteristics of $^{68}\text{Ge}/^{68}\text{Ga}$ generator, specified in Table 1, and applications of ^{68}Ga radionuclide in nuclear medicine [3, 6] it was decided to investigate more carefully the applications of this generator as a source of tracers for labeling of water phase in radiotracer experiments directed towards the determination of a RTD function.

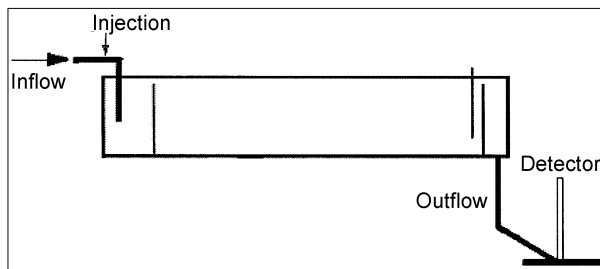
$^{68}\text{Ge}/^{68}\text{Ga}$ generator under investigations

Actually, the different $^{68}\text{Ge}/^{68}\text{Ga}$ generators are produced for medical purposes in few countries like Germany, China, India and others. In our investigations we used the generator produced in Germany with an activity of about 2 mCi (~ 70 MBq). The details of the generator construction and its characteristics are presented in [6]. The generator represents a glass column, containing a sorbent (TiO_2) with the ^{68}Ge radionuclide, placed into the shielding container. The elution of ^{68}Ga is realized by 5 ml of 0.1 M HCl solution.

The radiochemical tests of generator (analyses of gamma spectrum of eluate as a function of time) confirmed that the total activity of radioactive – in the majority the mother ^{68}Ge radioisotope – impurities was lower than 0.01%, thus from the industrial radiotracers methodology point of view we can state that the generator is a pure ^{68}Ga radioisotope source.

The applicability of $^{68}\text{Ge}/^{68}\text{Ga}$ generator as a source of radiotracer was tasted on a large scale laboratory installation – a model of rectangular settler of wastewater – (Fig. 1) with the volume $V = 2.93$ m³ and dimensions $L \times W \times H = 4.95 \times 1.3 \times 0.45$ m, where: L – length; W – width; H – height of the tank.

The radiotracer experiments were carried out according to the methodology recommended by the International Atomic Energy Agency [2]. In each experiment the RTD function of water phase was measured. As a reference tracer of water phase, the fluoresceine as representative of water tracer was used. Both the tracers – the eluate from the generator and the fluoresceine

**Fig. 1.** Scheme of industrial rectangular settler model.

– were injected simultaneously in the form of impulse function. The changing of fluoresceine concentration vs. time on the settler output was measured using a TURNER fluorimeter. The changing of radiotracer ^{68}Ga concentration on the output of the settler was measured continuously by the immersed in output water stream of NaI(Tl) scintillation detector connected with a field industrial radiometer (FIR).

Radiotracer experiments

In the first experiments the direct eluate from the $^{68}\text{Ge}/^{68}\text{Ga}$ generator, i.e. the Ga^{+3} ions in 0.1 M HCl solution was used as a radiotracer. The obtained experimental RTD functions, after background subtraction, radiotracer decay correction and normalization, for fluoresceine and gallium as tracers, are presented in Fig. 2. The water flow during the experiment was $Q \approx 3$ m³/h. The theoretical mean residence time $T = V/Q$, where: V – volume of tank (m³); Q – flow rate (m³/h) was $T = 0.895$ h.

The first and second central statistical moments of RTD functions represent mean residence time (MRT) of water in tank and standard deviation (SD) of residence time, respectively [2].

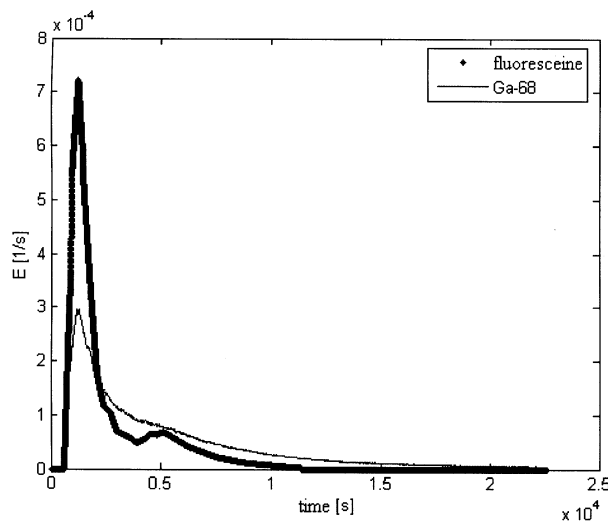
**Fig. 2.** Comparison of experimental RTD functions for fluoresceine and Ga-68 eluate directly from generator as tracers.

Table 2. The calculated MRT and theoretical MRT for experiment with the eluate directly from generator

Tracer	Theoretical MRT (h)	MRT (h)
Fluoresceine	0.895	0.72
Eluate directly from ⁶⁸ Ge/ ⁶⁸ Ga generator	0.895	1.43

The calculated values of MRT and *T* are presented in Table 2.

The practice of radiotracer experiments indicates that error of the calculated MRT value is in the 3–5% range.

The experimental MRT, for GaCl₃ as a tracer, is significantly bigger than the theoretical time *T* (what is impossible from physical and process engineering point of view). The results can be explained by a strong adsorption/desorption of tracer (Ga ions) on the walls of the tank during experiment what results in the long “tail” of RTD function and consequently, a big value of MRT. These phenomena exclude the taking of eluate directly from the generator as a suitable tracer of water phase in tracer experiments.

On the basis of literature data and experience of the ⁶⁸Ge/⁶⁸Ga generators application in medicine [5, 6], two chemical forms of Ga, i.e. macrocyclic chelates Ga-DOTA and -NOTA were proposed as a potential stable tracer of the water phase. The chemical structure of DOTA and NOTA are presented in Fig. 3.

A procedure for the postprocessing of generator eluate (0.1 M HCl solution with ⁶⁸GaCl₃) to obtain the Ga-DOTA and Ga-NOTA complexes was elaborated. The scheme of procedure is:

- Elution of GaCl₃ from the generator (about 5–7 ml of 0.1 M HCl solution).
- Addition of macrocyclic compounds DOTA or NOTA (0.01 M solution).
- Regulation of pH (about 3.5) by the addition of 0.01 M solution of ammonium acetate (CH₃COONH₄) and HCl.
- Heating of the mixture up to 90–95°C.
- Stabilization during 20–30 min.

After stabilization stage, the radiolabeling efficiency and stability evaluation was controlled by thin-layer

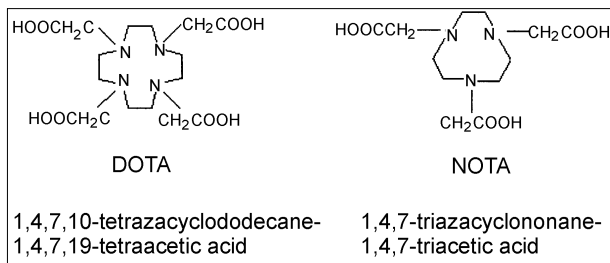


Fig. 3. The structures of DOTA and NOTA ligands.

Table 3. The calculated MRT and theoretical MRT for experiment, using fluoresceine and Ga-68 complexes with NOTA and DOTA as tracers

Tracer	Volume (m ³)	Flow rate (m ³ /h)	Theoretical MRT (h)	MRT (h)
Fluoresceine	3.1	3.23	0.96	0.83
Ga-68 + DOTA				0.89
Fluoresceine	3.1	3.19	0.97	0.67
Ga-68 + NOTA				0.65

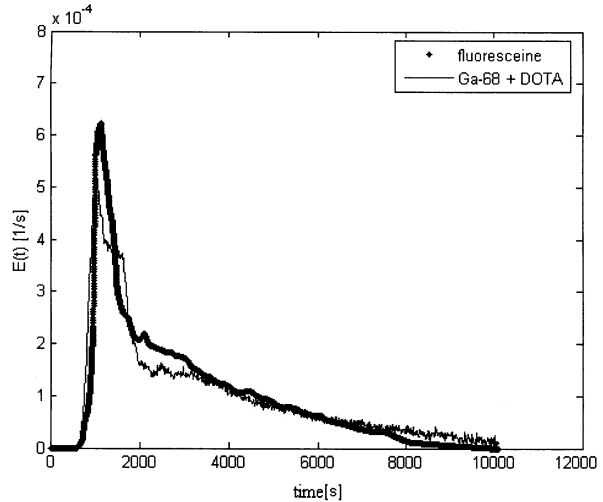


Fig. 4. Comparison of experimental RTD functions for fluoresceine and Ga-68 complexes with DOTA as a tracer.

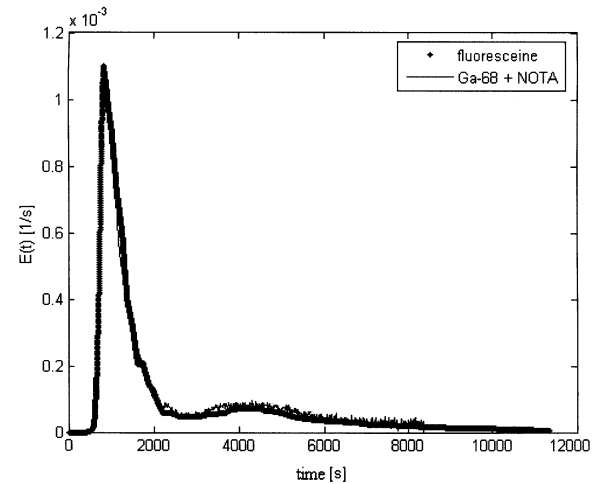


Fig. 5. Comparison of experimental RTD functions for fluoresceine and Ga-68 complexes with NOTA as a tracer.

chromatography (TLC). A mixture of H₂O and NH₃ in the ratio of 25 to 1 was used as the mobile phase. The ⁶⁸Ga-DOTA and ⁶⁸Ga-NOTA complexes moved from the solvent front (*R_f* = 0.8–1), while the free ⁶⁸Ga remained at the start (*R_f* = 0.0–0.3) where *R_f* is a retardation factor. It was stated that practically all ⁶⁸Ga – activity is bound with the complex.

A series of radiotracer experiments on the same model of settler with the application of Ga-DOTA and Ga-NOTA complexes as tracers of the water phase were carried out. Parallely, in each experiment the fluoresceine as a representative of the water tracer was used.

The obtained experimental RTD functions, after postprocessing are presented in Figs. 4 and 5.

The calculated MRT of RTD function, theoretical MRT, and flow conditions in the experiments are presented in Table 3.

In both cases the measured MRT is lower than the theoretical mean time (in accordance with the theory).

A better agreement (accordance) of the RTD function shape and measured MRT value – in comparison with the appropriate characteristics obtained for fluoresceine – is observed in the case of Ga-NOTA as a tracer.

Independently of the measured stability constants of the complexes, $\log K_{\text{Ga-DOTA}} = 21.33$ and $\log K_{\text{Ga-NOTA}} = 30.98$, indicated that the Ga-NOTA complex is stronger than the Ga-DOTA complex.

Conclusions

Comparison of the RTD functions obtained in radiotracers experiments with the application of Ga complexes and fluoresceine as tracers of the water phase indicated good accordance of the obtained results.

The proposed procedures of Ga ions complexation and preparation of macrocyclic chelates Ga-DOTA and Ga-NOTA can be recommended as postprocessing for obtaining stable water phase tracers on the basis of the $^{68}\text{Ge}/^{68}\text{Ga}$ generator eluate.

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